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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/770,418 | 02/04/2004 | Herve Le Mouellic | 2356.0053-09 | 1932 |

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| EXAMINER | |
|---|---|
| SHEN, WU CHENG WINSTON | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/770,418 | LE MOUELLIC ET AL. | |
| | Examiner | Art Unit | |
| | Wu-Cheng Winston Shen | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *24-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *24-101* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 24-101 are pending in the instant application.

### *Election/Restrictions*

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 24-28, 38-44, and 78, drawn to a DNA gene inactivation construct for homologous recombination in the genome of a mammalian cell, comprising recited sequences in a arranged order, including sequences encoding a leader sequences and is *fused in frame to a coding sequences encoding an expression product,* particularly a transmembrane coding region of the MHC antigen, for inactivation of a targeted gene locus, particularly a gene locus encoding a functional HMC antigen, wherein upon homologous recombination, said gene locus is inactivated, classified in class 536, subclass 23.1.

II. Claims 29-30 and 52-67, drawn to a DNA construct, *encoding no fusion protein before homologous recombination*, comprising recited sequences in 5' to 3' direction, including a region of homology to a target gene, a foreign promoter/enhancer joined to the first coding sequences that encodes a first gene product, particularly a first epitope that binds a ligand for detection, said target gene comprising a second coding sequence encoding a second gene product, particularly a second epitope, and said target gene including a gene encoding a subunit of an MHC antigen and a gene encoding a protein that upregulates expression of MHC antigen, wherein upon homologous recombination, of said DNA construct into a genome, a recombinant, fusion protein, particularly secreted fusion protein, comprising said first gene product and part or

all of said second gene product is expressed in targeted cells, and wherein, as a result of homologous recombination, at least one functional copy of the target gene is not expressed, particularly one functional MHC antigen or protein associated with expression of MHC antigens is not expressed, classified in class 536, subclass 23.1.

III. Claims 31-37, drawn to A DNA construct comprising DNA encoding a transcriptionally and translationally impaired positive selectable marker gene *fused in frame to the transmembrane coding region of an integral membrane protein receptor for a cytokine* that upregulates the expression of MHC antigen; wherein the expression product of said DNA is a fusion protein comprising a functional selectable marker expressed on the cytoplasmic side of said membrane, classified in class 536, subclass 23.1.

IV. Claims 45-51, drawn to a DNA gene inactivation construct, *encoding no fusion protein either before or after homologous recombination*, for homologous recombination in the genome of a mammalian cell having a recipient DNA sequence, wherein said recipient DNA sequence comprises complementing DNA comprising a first nucleotide sequence and a second nucleotide sequence downstream of said first nucleotide sequence, wherein the DNA gene inactivation construct comprises: (1) a third nucleotide sequence homologous to said first nucleotide sequence; (2) a fourth nucleotide sequence homologous to said second nucleotide sequence; and (3) a DNA sequence heterologous with respect to said recipient DNA sequence, wherein said heterologous DNA sequence is between said third and said fourth nucleotide sequences and said heterologous DNA sequence comprises a first insertion DNA sequence and a second insertion DNA sequence, wherein said first insertion DNA sequence comprises a first coding sequence that encodes a first product that does not confer resistance to a selection agent

involved in the selection of transformants, and said second insertion DNA sequence comprises a second coding sequence that encodes a second product that confers resistance to a selection agent involved in the selection of transformants, wherein upon insertion of said heterologous DNA sequence between said first and said second nucleotide sequences in said recipient DNA sequence by homologous recombination with said third and said fourth nucleotide sequences, to thereby provide a mammalian cell containing the recombinant DNA sequence, said second coding sequence is operably linked to a regulatory sequence allowing the expression of said second product in said mammalian cell, classified in class 536, subclass 23.1.

V. Claims 68-77, drawn to A DNA construct, *encoding two distinct gene products,* comprising a first DNA sequence and a second DNA sequence, wherein said first DNA sequence comprises a first coding sequence that encodes a first gene product that does not confer resistance to a selection agent involved in the selection of transformants, and said second DNA sequence comprises a second coding sequence that encodes a second gene product that confers resistance to a selection agent involved in the selection of transformants, wherein the second DNA sequence is downstream of the first DNA sequence, wherein the expression product of said DNA construct comprises the second product that confers resistance to a selection agent involved in the selection of transformants, in functional form, classified in class 536, subclass 23.1.

VI. Claims 79-101, drawn to a method for modifying a target DNA sequence in a mouse embryonic stem cell comprising recited steps, classified in class 800, subclass 21.

Additionally, Groups I-V named above are subject to further restriction. Applicant is required to further elect a specific combination of (a class of MHC antigen --- e.g. claims 25; a gene locus of a subunit MHC antigen or a gene encoding a protein that upregulates expression of MHC antigen --- claims 26; a selectable resistance gene --- e.g. claims 27-28; a target gene --- e.g. claim 33; a receptor for a cytokine that regulates the expression of MHC antigen --- e.g. claim 35; a integral membrane protein --- e.g. claim 37; a receptor for an infectious or toxic agent --- e.g. claims 41-44, 48-51, 55, 62, 72; a receptor --- e.g. 56-58, 63-65, 73-75) from (the claim, table, etc), [or a specific combination of... to which the claims will be limited]. This is **NOT** an election of species. Structurally distinct DNA polynucleotide sequences encoding different polypeptides are distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequences are presumed to represent an independent and distinct invention, subject to restriction requirement pursuant to 35 USC 121 and 37 CFR 1.141. By statute, "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." 35 U.S.C. 121. Pursuant to this statute, the rules provide that "[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant... to elect that invention to which his claim shall be restricted." 37 CFR 1.142 (a). See also 37 CFR 1.141(a). It is noted that searching more than one of the claimed patentably distinct sequences represents a serious burden for the office.

Groups I-V are directed to a DNA construct directed to recited coding sequences in a particular arrangement. Groups I-V are patentably distinct one from each other because the DNA construct of Group I comprising sequences encoding a leader sequences and is fused in frame to a coding sequences encoding an expression product, particularly a transmembrane coding region of the MHC antigen; the DNA construct of Group II encodes no fusion protein before homologous recombination; the DNA construct of Group III encodes transcriptionally and translationally impaired positive selectable marker gene fused in frame to the transmembrane coding region of an integral membrane protein receptor for a cytokine that upregulates the expression of MHC antigen; the DNA construct of Group IV encodes no fusion protein either before or after homologous recombination; and the DNA construct of Group V encodes two distinct gene product, comprising a first DNA sequence and a second DNA sequence, wherein said first DNA sequence comprises a first coding sequence that encodes a first gene product that does not confer resistance to a selection agent involved in the selection of transformants,

Groups I-V are distinct from Group VI because Groups I-V are directed to a DNA construct for either inactivation or modification of a gene in a mammalian cell whereas Group VI is directed to a method for modifying a target DNA sequence in a mouse embryonic stem cell comprising recited steps. The structures of DNA constructs of Group I-V are not obvious over the steps and technical considerations of the method of Group VI.

The search for claims in Group I-VI is distinct one from each other and not co-extensive and thereby presents search burdens on the examiner.

3. Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

4. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30

PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Ram Shukla, can be reached on (571) 272-0735. The fax number for TC 1600 is (571) 273-8300. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Wu-Cheng Winston Shen

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

**Initially attempted**